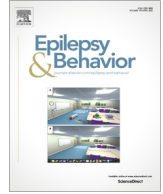




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COVID-19 pandemic influence on epilepsy course in pediatric patients

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ABSTRACT

Introduction: In 2020, Coronavirus Disease 2019 (COVID-19) was declared as a global pandemic. Self-reported stress, anxiety, and insomnia, which are believed to be common triggers for epilepsy, are more likely to occur. We aimed to establish the influence of COVID-19 pandemic itself on changes in the daily life routine related to pandemic on epilepsy course in pediatric patients. The unique form of clinical care which is telemedicine was also taken into consideration. We wanted to evaluate patients' satisfaction with telemedicine and if changing stationary visits into telemedicine influenced epilepsy course in our patients.

Methods: Patients, who attended developmental neurology outpatient clinic in the period March–December 2020 were collected. As patients were minors, legal guardians were asked to fill out the questionnaire. Patients were divided according to the outcome into three groups: those with a worsened, stable, or improved course of epilepsy during the pandemic. Appropriate statistical tests for two-group and multi-group comparisons have been implemented. Post hoc *p* values were also calculated.

Results: Four hundred and two questionnaires were collected. Most of the patients had a stable course of epilepsy during the pandemic; in 13% of participants an improvement has been observed, worsening of the disease was seen in 16% of patients. Age, sex, type of epilepsy, number of seizure incidents before pandemic, and duration of the disease had no statistically significant connection with changes in the course of the disease. Behavioral changes and altered sleep patterns were found to be more common in the worsened group.

Fifty-eight percent of patients were satisfied with telemedicine. Poorer satisfaction was connected with less frequent visits, cancellation of scheduled appointments, and lack of help in case of need in an emergency situation.

Conclusion: Epilepsy course in pediatric patients seems to be stable during COVID-19 pandemic. Sleep disturbances and changes in a child's behavior may be related to increase in seizure frequency. Telemedicine is an effective tool for supervising children with epilepsy. Patients should be informed about possible ways of getting help in urgent cases.

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1. Introduction

On March 11th, 2020 the World Health Organization declared the outbreak of Coronavirus 2019 (COVID-19) as a global pandemic. Implications that followed this declaration were

devastating to economic, social, and health factors. The consequences of the novel coronavirus on physical as well as mental health are currently a major concern [1]. Social distancing was implemented as the main viral transmission prevention technique, leading to loneliness, which in turn may further result in depression, anxiety, and chronic stress [2,3]. To avoid direct contact with patients, for their safety and the safety of healthcare providers, clinical care had to be partially shifted toward telemedicine [4].

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Epilepsy is a chronic disease and requires frequent follow-up consultations to provide adequate patient care [5]. Prior studies suggest that COVID-19 may cause worsening of preexisting neurological disorders, some authors reported an increased number of seizures during the pandemic and described de novo seizures in COVID-19 patients [6–8]. Although no clear connection between COVID-19 and epilepsy has been established yet, it is essential to evaluate the effects of the pandemic on common diseases. The pandemic caused an increased occurrence of anxiety, depression, insomnia, and, not surprisingly, changes in sleep pattern and an increase in self-reported stress, which are believed to be common triggers for epilepsy [3,9,10]. In our study, we aimed to establish the influence of COVID-19 pandemic itself on changes in the daily life routine related to pandemic on epilepsy course in pediatric patients. We wanted to evaluate seizure frequency before the pandemic outbreak and during the pandemic and find reasons for possible changes in epilepsy course. The unique form of clinical care which is telemedicine was also taken into consideration as it was significantly different from the standard medical care provided in pediatric patients affected by epilepsy. We wanted to evaluate patients' satisfaction with telemedicine and if changing stationary visits into telemedicine influenced epilepsy course in our patients.

2. Materials and methods

The study was designed as a cross-sectional study. Medical records of patients with an established diagnosis G.40 in International Classification of the Disease (ICD) or diagnosis “epilepsy” according to International League Against Epilepsy (ILAE) definition [11], who attended the developmental neurology outpatient clinic in the period between March 2020 and December 2020 were collected. The study was conducted in January 2021, by this time period given above corresponded with the time of the pandemic in Poland. The exclusion criteria were: unconfirmed diagnosis of epilepsy and diagnosis made in 2020, as in those patients, the comparison of epilepsy course before and after the pandemic outbreak was impossible. Patients with only one provoked episode of seizure in the past attributed to transient states like fever, hemorrhage, and infection were also excluded. Informed consent from the bioethical commission was obtained. Questionnaires were collected using the telephone by one of the research team members. As patients were minors, legal guardians were asked to answer the questions. The consent for participating in the survey was obtained from each participant. The language of the questionnaire was Polish. For publication purpose, the questionnaire and answers were translated into English by a university employee, specialized in medical English. All answers were collected anonymously. The study design is presented in Fig. 1.

The questionnaire was designed by a developmental neurologist and neuropsychologist (MZ and MMB), experienced in epilepsy healthcare. It consisted of four sections: demographic data, epilepsy course and treatment, medical care during the pandemic, and additional information. The questionnaire is presented in the appendices. Control of epilepsy was assessed in 2019 and 2020 separately considering the frequency of seizure episodes per month. A separate question was asked about the change in the course of epilepsy during the pandemic. If the answer “no change” was marked, the patient in question was placed in the group “Stable”. Answering “yes” in the questionnaire resulted in an additional question: “What change was observed?”. The following answer possibilities were given: 1. more frequent occurrence of seizures, 2. less frequent occurrence of seizures, 3. more severe or longer epilepsy episodes, 4. less severe or shorter epilepsy epi-

sodes, and 5. occurrence of a new type of seizures. Participants, who responded 1., 3., or 5. were placed in a group consisting of patients with a “worsened course of epilepsy”, persons, who responded 2. or 4. were placed in the group which experienced an “improved course of epilepsy”.

2.1. Statistical analysis

Raw data were collected in Excel spreadsheets (Microsoft, USA). Statistical analysis was performed using the STATISTICA 10.0 software (StatSoft Inc., USA). All of the quantitative variables were tested using the Kolmogorov–Smirnov test, for meeting the criteria of a normal distribution (Gaussian distribution). Depending on whether the variable met the normality condition, appropriate statistical tests were applied at further stages. Continuous data were presented as median and quartiles if they did not meet the conditions of the normal distribution. For comparisons between two groups the parametric *T*-test or nonparametric Mann–Whitney *U* Test, was used. For the comparison of multiple groups, the Analysis of variance (ANOVA) test (for variables of parametric distribution) or Kruskal–Wallis test (variables of non-parametric distribution) was used. For comparing qualitative survey data Pearson's chi-square test (with appropriate Yates' Correction for small observed frequencies) was used. In the next step, the post hoc Chi-square analysis was performed, based on adjusted residuals of each variable.[12] The Bonferroni correction was also implemented, as this adjustment is commonly used to protect from Type I error in multiple comparisons. The level of statistical significance in calculations was set at the $p < 0.05$ or correspondingly lower, if determined by the Bonferroni correction.

3. Results

We identified 622 patients in total. Fifty-two patients were excluded due to one of the exclusion criteria. Seventy-eight guardians refused to take part in the survey, fifty-four did not answer the telephone (three contact attempts were made), fourteen did not finish the questionnaire, and in twenty-two cases the contact number in the medical records turned out to be incorrect. Eventually, 402 questionnaires were collected with a response rate of 70.53%.

3.1. Background and demographic data

All demographic data are detailed in Table 1.

3.2. Changes in epilepsy control

Characteristic of each group is presented in Table 2.

Participants were divided into three groups, based on the course of their disease during the COVID-19 pandemic: Improved, Stable (unchanged epilepsy course), and Worsened. Two hundred eighty-four patients (70.6%) were in the “Stable” group, Changes in the epilepsy course were found in one hundred eighteen patients (29.4%).

Sixty-six (16.4%) patients experienced worsening of the course of epilepsy (“Worsened”). When asked to define the change: 25 declared more frequent occurrence of seizures, 10 more severe or longer seizures, 10 patients had new type of seizures, and 21 claimed to have more than one mentioned above. Patients were asked about the month, in which poorer control appeared. The most frequently named month was November 2020 (21.52%), although no statistically significant correlation was found. In this group of children, seizure frequency in 2019 compared to 2020

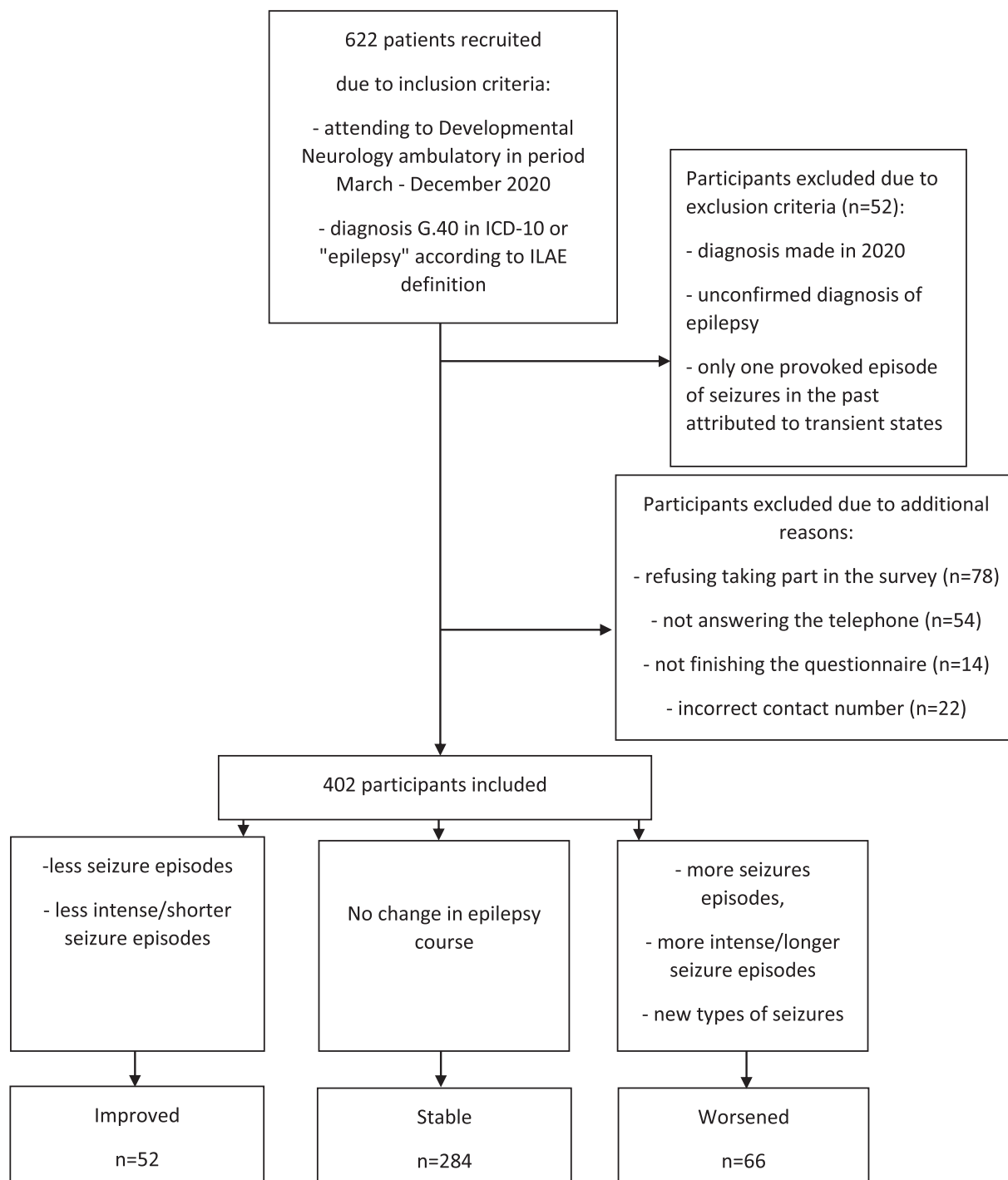


Fig. 1. Study design.

varies, as in 2020 patients had statistically more seizures compared to the year before. This significant spread was especially evident in the subgroups experiencing more than 20 seizures and not experiencing any seizures.

Fifty-two patients (12.9%) were assigned to the "Improved" group. When asked to define the change: 30 declared less frequent occurrence of seizures, 5 less severe or shorter seizures, and 17 claimed to have both. In this group of children, seizure frequency in 2019 compared to 2020 varies, as in 2020 patients had statistically fewer seizures compared to the year before.

3.3. Factors associated with changes in epilepsy control

All factors associated with epilepsy course are presented in Table 3.

In the Improved group, 76.9% of the patients (40/52) attended school/kindergarten, in the group Stable – 90.1% (256/284), and in the group Worsened 86.4% (57/66). School problems during the pandemic such as worse school grades or lack of concentration were noticed in 31.5% of patients, no significant differences were found between groups.

Table 1
Demographic data.

	Total, N = 402
Females, N (%)	167 (41.54%)
Males, N (%)	235 (58.46%)
Age median, years (Q1–Q4)	11 (6–14)
Duration of epilepsy, years (Q1–Q4)	5 (3–8)
Place of residence, N (%)	
Village	142 (35.32%)
city up to 50,000 habitants	84 (20.9%)
city 50 000–100,000 habitants	25 (6.22%)
city 100,000–500,000 habitants	17 (4.23%)
city over 500,000 habitants	134 (33.33%)
Distance from the place of residence to the outpatient clinic, where the patient used to have epilepsy-control visits, N (%)	
0–50 km	250 (62.19%)
51–100 km	91 (22.64%)
over 100 km	61 (15.17%)
Attending to school/preschool, N (%)	
Yes	353 (87.81%)
No	49 (12.19%)
Epilepsy type, N (%)	
Focal	156 (38.81%)
Generalized	170 (42.29%)
Both	76 (18.91%)

Changes in a child's behavior during pandemic were seen by 33.3% of parents. The most common problems were irritability (78.4%), avoiding contact with the household members (19.4%), fear of leaving the house (18.7%), and presence of somatic problems such as headaches (17.2%). Statically significant differences were noted between groups as children in the group “Improved” did not experience changes in behavior as often as other groups.

Table 2
Characteristic of groups.

Variable	Improved N = 52 12.94%	Stable N = 284 70.65%	Worsened N = 66 16.42%	p
Age, median years (Q1–Q4)	10 (4–14.5)	11 (7–14)	8 (5.5–14)	p = 0.33
Duration of epilepsy, years (Q1–Q4)	4 (3–9)	5 (3–8)	6 (3–10)	p = 0.71
Gender, N (%)				
Males	32 (61.54%)	166 (58.45%)	37 (56.06%)	p = 0.83
Females	20 (38.46%)	118 (41.54%)	29 (43.94%)	
Place of residence, N (%)				
Village	20 (38.46%)	96 (33.80%)	25 (37.88%)	
city up to 50,000 habitants	9 (17.31%)	63 (22.18%)	12 (18.18%)	
city 50,000–100,000 habitants	2 (3.85%)	18 (6.34%)	5 (7.58%)	p = 0.90
city 100,000–500,000 habitants	3 (5.77%)	13 (4.58%)	1 (1.52%)	
city over 500,000 habitants	18 (34.62%)	94 (33.10%)	23 (34.85%)	
Epilepsy type, N (%)				
focal	16 (30.77%)	115 (40.49%)	26 (39.39%)	
generalized	23 (44.23%)	123 (43.31%)	22 (33.33%)	p = 0.11
both	13 (25.00%)	46 (16.20%)	18 (27.27%)	
Frequency of seizure episodes per year in 2019, N (%)				
None	5 (9.61%)	147 (51.76%)	17 (25.76%)	
1–2 (once per year/half year)	6 (11.53%)	49 (17.25%)	9 (13.63%)	
3–5	9 (17.31%)	20 (7.04%)	9 (13.63%)	
6–12 (once per month)	5 (9.61%)	17 (5.99%)	6 (9.52%)	p = 0.08
13–20	5 (9.61%)	15 (5.28%)	7 (10.61%)	
21–100	8 (15.38%)	11 (3.87%)	3 (4.56%)	
over 100 (daily)	14 (26.92%)	25 (8.80%)	15 (22.73%)	
Frequency of seizure episodes per year in 2020, N (%)				
None	12 (23.08%)*	173 (60.91%)*	0 (0.00%)*	p < 0.05
1–2 (once per year/half year)	6 (11.54%)	39 (13.73%)	11 (16.67%)	(Bonferroni
3–5	6 (11.54%)	17 (5.98%)	8 (12.12%)	correction
6–12 (once per month)	5 (9.62%)	13 (4.58%)	6 (9.10%)	p = 0.0024)
13–20	4 (7.69%)	10 (3.52%)	10 (15.15%)	
21–100	9 (17.31%)	11 (3.87%)*	14 (21.21%)*	
over 100 (daily)	10 (19.23%)	21 (7.39%)*	17 (25.76%)*	

* Significant p value in post hoc analysis (after Bonferroni correction).

Sleep disturbances were noticed by 30.5% of guardians. The most common were problems with falling asleep (45.2%), waking at night (36.6%), disturbances of the circadian rhythm (33.9%), longer sleep time (23.4%), shorter sleep time (17.7%), and insomnia (16.1%). Statically significant differences were noted between groups as children in the group “Improved” did not experience changes in behavior as often as other groups.

3.4. Infection and epilepsy

41.7% of patients suffered from any kind of infection during the COVID-19 pandemic, no differences between the groups were seen. Twenty-nine children suffered from COVID-19 infection, confirmed by polymerase chain reaction test (PCR). Symptoms declared were: fever above 38 degrees of Celsius (10/29), taste and olfactory disturbances (7/29), headaches (7/29), fatigue (6/29), cough (5/29), muscle pain (4/29), and asymptomatic (6/29). Four parents claimed COVID-19 infection led to the worsening of the control of epilepsy, all of them noticed more frequent occurrence of seizure episodes and two more reported an increase in the intensity of epileptic seizures along with a manifestation of an additional, new type of seizures. Three of those children had fever above 38 degrees of Celsius, one had only taste and olfactory disturbances.

3.5. Medical care

Telemedicine appointments were conducted in all three groups. “Improved” group declared those appointments were as effective as standard medical appointments more often than other groups, although no statistical significance was achieved ($p = 0.07$).

Table 3
Factors associated with changes in epilepsy course.

Variable	Improved N = 52	Stable N = 284	Worsened N = 66	p
<i>Did you observe any sleep disturbances in your child during the COVID-19 pandemic?, N (%)</i>				
Yes	22 (42.31%)	68 (23.94%)*	33 (50.00%)*	<i>p</i> < 0.001* (Bonferroni correction <i>p</i> = 0,0083)
No	30 (57.69%)	216 (76.06%)*	33 (50.00%)*	
<i>Did you notice changes in your child's behavior during the COVID-19 pandemic?, N (%)</i>				
Yes	19 (36.54%)	77 (27.11%)*	37 (56.06%)*	<i>p</i> < 0.001* (Bonferroni correction <i>p</i> = 0,0083)
No	33 (63.54%)	207 (72.89%)*	29 (43.94%)*	
<i>Did you notice any school problems in your child during COVID-19 pandemic?, N (%)</i>				
Yes	21 (40.38%)	85 (29.93%)	22 (33.33%)	<i>p</i> = 0.31
No	31 (59.62%)	199 (70.07%)	44 (66.67%)	
<i>Did your child have any infection during the COVID-19 pandemic?, N (%)</i>				
Yes	22 (42.31%)	118 (46.46%)	26 (39.39%)	<i>p</i> = 0.94
No	30 (57.69%)	166 (58.45%)	40 (60.61%)	
<i>Was the frequency of medical consultations comparable to the frequency before the pandemic?, N (%)</i>				
Yes	41 (78.85%)	219 (77.11%)	40 (60.60%)*	<i>p</i> < 0.001* (Bonferroni correction <i>p</i> = 0,0055)
no - more frequently	2 (3.85%)	11 (3.87%)*	14 (21.21%)*	
no - less frequently	9 (17.31%)	54 (19.01%)	12 (18.18%)	
<i>Was any of medical appointment conducted in a form of a telemedicine?, N (%)</i>				
Yes	46 (88.46%)	240 (84.50%)	55 (83.33%)	<i>p</i> = 0.79
No	6 (11.11%)	44 (15.49%)	11 (16.67%)	
<i>Do you think that a telemedical consultation was as effective as a stationary visit?, N (%)</i>				
Yes	31 (67.39%)	143 (59.58%)	25 (45.45%)	<i>p</i> = 0.07
No	15 (32.61%)	97 (40.42%)	30 (54.55%)	

*Significant p value in post hoc analysis (after Bonferroni correction).

Changes in medical appointment frequency during pandemic were more often declared in the "Worsened" group ($p = 0.001$).

Eighty-one of participants claimed difficulty with drug supplies during the pandemic; 95.1% of them reported no drug availability in drug stores, the other 4.9% had a problem with reaching pharmacy because of quarantine.

3.6. Medical care and telemedicine

Three hundred forty-one (84.8%) patients had at least one telemedicine appointment. There was no statistically significant change in frequency of seizure episodes between 2019 and 2020 in those patients; 199 of them (58.4%) stated online visits were as efficient as the standard medical appointments. In 82.9% of cases in this group consultations were performed as

often as before the pandemic; 142 of the patients (41.6%) found telemedicine less satisfactory and in this group in 62.0% of cases the visits took place as often as before the pandemic. A statistically significant correlation between satisfaction with telemedicine and frequency of appointments was found ($p = 0.0001$). In 13.48% of unsatisfied patients neurologists canceled a scheduled appointment, compared to 4.52% of patients in the satisfied group ($p = 0.003$). About one-quarter of patients in each group required urgent hospitalization or consultation in addition to the scheduled appointments, almost all patients (97.83%) from the satisfied group managed to get help, while for 32.50% of patients from the unsatisfied group no medical support was provided ($p = 0.001$). There was no correlation between patient's satisfaction and distance to the clinic.

Further information about the groups is presented in Table 4.

Table 4
Telemedicine satisfaction.

	Satisfied with telemedicine N = 199 58.36%	Not satisfied with telemedicine N = 142 41.64%	p
<i>Was the frequency of medical consultations comparable to the frequency before the pandemic?, N(%)</i>			
yes, N (%)	165 (82.91%)	88 (61.97%)	<i>p</i> < 0.001*
no, N (%)	34 (17.09%)	54 (38.03%)	
<i>What was the change in frequency of appointments?, N(%)</i>			
more frequent, N (%)	16 (47.06%)	11 (20.37%)	<i>p</i> = 0.01*
less frequent, N (%)	18 (52.94%)	43 (79.63%)	
<i>Distance from the place of residence to the outpatient clinic, where the patient used to have epilepsy-control visits, N(%)</i>			
up to 50 km	126 (63.32%)	91 (64.08%)	<i>p</i> = 0.81
50–100 km	47 (23.62%)	30 (21.13%)	
more than 100 km	26 (13.07%)	21 (14.79%)	
<i>Has the neurologist ever canceled a scheduled appointment?, N(%)</i>			
yes, N (%)	9 (4.52%)	19 (13.48%)	<i>p</i> = 0.003*
no, N (%)	190 (95.48%)	123 (86.61%)	
<i>Was there a need for urgent hospitalization or medical advice during the pandemic in addition to scheduled, regular visits?, N(%)</i>			
yes, N (%)	48 (24.12%)	40 (28.17%)	<i>p</i> = 0.39
no, N (%)	151 (75.88%)	102 (71.83%)	
<i>If yes, did you manage to get help?, N(%)</i>			
yes, N (%)	45 (97.83%)	27 (67.50%)	<i>p</i> < 0.001*
no, N (%)	1 (2.17%)	13 (32.50%)	

* Statistically significant results.

4. Discussion

4.1. Impact on epilepsy course

The study investigated the effect of the COVID-19 pandemic on epilepsy course in pediatric patients and, according to our knowledge, is the first study, which correlates changes in epilepsy course during COVID-19 with changes in daily routine and in epilepsy healthcare in pediatric population. In most of our patients, the disease had a stable course. If the course has changed, worsening (16.4%) was observed slightly more commonly than improvement (12.9%). Groups did not differ in the median age of children, epilepsy type, or duration of the disease. Furthermore, seizure frequency before pandemic was also similar in each group. A few studies investigated the impact of the COVID-19 pandemic on epilepsy course in adults. Worsening was observed in 17–25% of the adult population [13–15]. It correlated with more stress and anxiety in those patients. COVID-19 pandemic has an undeniable influence on the mental health of the patients. More than half of adults experiencing epilepsy declared an increase in stress level during the pandemic [10]. Adults expressed their fear of losing a job, financial problems, hospitalization, or concern of loved ones [14]. However, we need to remember that patients in our study had a median age of 11 years. The concerns mentioned above are usually irrelevant for children. Our results are compatible with Trivisano et al.'s study, which resulted in seizure frequency during COVID-19 being unchanged in 66.5% of pediatric population, increased in 13.3%, and decreased in 20.3% of children [16]. The situation of global lockdown with closed schools, online classes, and online exams could provide a less stressful environment for children. Studies suggest that the well-being of young children (age group 6–10 years) did not change during the time of the pandemic. In addition, almost half of the parents claimed improvement of their parent–child relationship during lockdown [17]; furthermore, most of the caregivers do not report that pandemic had a negative influence on the mental health of their children [18].

In our survey, subjects, who declare worsening in seizure control were more likely to have sleep disturbances and new changes in the child's behavior like irritability. Most commonly mentioned problems were: troubles falling asleep, waking at night, and disturbances of the circadian rhythm. Undeniably, a lack of daily routine could influence those aspects. It may reflect in hyperactivity and, in consequence, irritability, anger, or avoiding contact with household members [17]. Some children can be more susceptible to changes in daily routine, which can affect their disease. Moreover, children are susceptible to emotions present at home. Even if the global healthcare crisis did not influence them directly, it might have had an impact on their parents. An increase in parental stress could directly interfere with the life quality of adolescents [19]. For this reason, doctors should evaluate stress level in young patients and also their caregivers, asking questions about sleep, activities, and mood. Some patients and their families might require psychological support. General advice about sleep, a healthy lifestyle, and maintaining physical activity should be given [20]. Future studies should investigate stress levels not only in children but also in their household members.

Almost 13% of patients had improvement in the course of their disease. No differences comparing this group to the rest of the patients were found. Epilepsy has a natural tendency to a sinusoidal course, consisting of remissions and exacerbations. According to Sander et al. about 70–80% of patients will go into long-term remission, usually within the first 5 years [21]. The question remains – is it attributable to the COVID-19 pandemic or just a natural course of epilepsy? Follow-up of those patients could be useful for answering whether the improvement was temporary

or not and if the frequency of seizures returns to baseline after the pandemic.

4.2. Infections

Infections can be a potential trigger of seizures in children, especially combined with fever [22]. In our study, 29 patients were diagnosed with COVID-19. Four parents declared worsening of the course of epilepsy related to COVID-19 infection. Three of those children suffered from high fever, which can be an independent seizure trigger, despite SARS-CoV-2 virus infection. The relation between COVID-19 and epilepsy is not clear [23]. The disease itself causes a systematic inflammatory reaction presenting with a high fever and symptoms from the respiratory tract. The influence of the SARS-CoV-2 virus on the brain and a potential mechanism of epilepsy is still controversial. In literature, case reports and case series of patients with new-onset seizures (focal or general) in the course of COVID-19 infection are reported [7]. The potential mechanism involves the entry of pro-inflammatory cytokines into the nervous system, an increase in glutamate and aspartate, and a reduction in gamma-aminobutyric acid (GABA) levels [24]. All of these can provoke more seizures in patients affected by epilepsy. More data should be collected to establish an undeniable connection.

4.3. Medical care during COVID-19 pandemic

The great concern of this report is access to healthcare providers and drug supplies during the pandemic. Proper antiepileptic therapy is crucial for a seizure-free course of epilepsy. In the consensus published in *Neurology* in May 2020 stockpiling of medication is discouraged [20]. However, 20% of responders had problems with drug availability during the pandemic, due to lack of medications in pharmacies and being on quarantine. Considering those situations, it may be useful for patients to have supplies of appropriate medications for upcoming weeks. Taking medication regularly is crucial. Every pause could be catastrophic for seizure control.

Telemedicine has a great potential for increasing the availability of patient care. Current communication tools provide access to healthcare regardless of the distance from the hospital and patient's mobility. One of its major limitations is the reduced ability to perform a physical examination; however, in epilepsy treatment, especially in follow-up management physical examination is rarely necessary [9,25]. Prior studies of adult subjects showed that telephone consultations were effective and efficient in providing remote epilepsy care [13,20]. Moreover, telemedicine has the potential of addressing limited resources and improving access to people with epilepsy across the globe [26,27]. In our study, 58% of subjects consider the effectiveness of epilepsy treatment via telephone consultation as qualitatively equal to a stationary visit in the outpatient clinic. No significant changes in the epilepsy control were noted in both, satisfied and dissatisfied patients. Teleconsultation did not influence epilepsy control, comparing the frequency of seizure episodes in 2019 and 2020. We assumed that patients living at a great distance from the clinic would be more satisfied with telemedicine, but no correlation was found. Mentioned results suggest that telemedicine is a good, sufficient tool, especially from the medical point of view. For a doctor, the major point in epilepsy management is a stable seizure frequency, which, according to our results, may be achieved by telemedicine. Long-term epilepsy management is mainly based on a detailed interview with the patient or patient's caregivers, which can be potentially accomplished by a phone call. Previous studies support those statements as telemedicine consultations were successfully utilized as an important tool for epilepsy management regardless of epilepsy type, etiology, seizure frequency, comorbidities, and patients' residential areas [28]. It was also used with a success in

diagnosis and managing childhood absence epilepsy [29]. Telemedicine may also provide high satisfaction and economic benefits in the future, after the pandemic [30]. However, Kubota et al. described a connection between telemedicine appointments and a higher incidence of status epilepticus [31]. Results of van Wrede et al. pointed out more potential disadvantages such as lack of personal contact and diagnostics (electroencephalogram [EEG] recordings, blood analysis) and, eventually, about three-fourth of the participants wished to have further appointments face-to-face [32]. Telemedicine has great potential, but it may not be enough if it is the only tool for supervising the patient, which should be considered by doctors.

Although previous studies reported high satisfaction of the patients with telemedicine, in our study 40% of the patients were not satisfied [33]. One of the major reasons for dissatisfaction might have been the lower frequency of consultations as a group of dissatisfied patients reported less frequent visits than before the pandemic. Canceling teleconsultation by the neurologist was another reason for the poorer satisfaction. Those disadvantages could be easily removed by regularly scheduled visits. Alarming is the fact that one-third of unsatisfied patients did not manage to get help when the need for an urgent consultation appeared. In the era of COVID-19, many emergency departments and hospitals are limited only to COVID-19-positive patients. Patients with chronic diseases should be informed about possible ways to contact doctors beyond scheduled appointments. Doctors should ensure patients, that despite the tough time of the pandemic, their disease is still important and fully cared for.

Our study has its limitations. The study is a cross-sectional study, which cannot determine the causality between the associated factors and is based on the univariate analysis, which cannot consider the confounding factors. The questionnaire has no validation as there is no validated questionnaire on this topic. As the patients were minor, the questionnaires were filled out by their legal guardians, the questions about subjective feelings about stress had to be excluded. The answers were collected by phone call. Although the data were saved anonymously, responders might have felt embarrassed or not comfortable with answering honestly, directly to the employee of the clinic. Nonetheless, neurologists, who directly treat patients did not take part in collecting questionnaires. The seizure frequency was based on caregivers' answers. The questions were asked retrospectively and were related to the period of seven months, so recall bias was unavoidable; however, according to our experience, parents of children with epilepsy are very focused on their child's disease and can easily observe changes in the course of the epilepsy. We advise them to keep "seizure diaries", so in many cases we could evaluate carefully frequency of seizure.

5. Conclusion

Epilepsy course in pediatric population seems to be stable during COVID-19 pandemic. Sleep disturbances and changes in a child's behavior may be related to increase in seizure frequency. Problems with pharmacy stores supplies and being on quarantine may cause difficulty with the availability of medications. Teleconsultations seem to be an efficient tool for providing healthcare to children with epilepsy. Regularity of consultations should be kept, and another date should be set in case of cancellation. Patients should be informed about possible ways of getting help in case of urgent medical needs.

Declaration of Competing Interest

None.

Appendix A. Questionnaire

Demographic data

- 1 Gender of the patient:
 - a. Male
 - b. Female
2. Age
.....
3. Place of residence:
 - a. Village
 - b. City with up to 50 000 inhabitants
 - c. City with 50 000 to 100 000 inhabitants
 - d. City with 100 000 to 500 000 inhabitants
 - e. City with over 500 000 inhabitants
4. Distance from the place of residence to the outpatient clinic, where the patient used to have epilepsy-control visits:
 - a. 0–50 km
 - b. 51–100 km
 - c. Over 100 km
5. Did the patient attend preschool/school?
 - a. Yes
 - b. No
- 5.1 If yes, did the patient attend preschool/school during the pandemic as well?
 - a. Yes
 - b. No

Epilepsy course and treatment

1. In what year was epilepsy diagnosed?
.....
2. What is the type of the epilepsy?
 - a. Focal
 - b. General
 - c. Both – focal and general
3. How many epileptic episodes occurred in total in the year 2019?
 - a. None
 - b. 1–2 (once in half a year)
 - c. 3–5
 - d. 6–12 (once a month in average)
 - e. 13–20 (more than once per month)
 - f. 21–100
 - g. More than 100 (epileptic episodes daily or almost daily)
4. How many epileptic episodes occurred in total in the year 2020?
 - a. None
 - b. 1–2 (once in half a year)
 - c. 3–5
 - d. 6–12 (once a month in average)
 - e. 13–20 (more than once per month)
 - f. 21–100
 - g. More than 100 (epileptic episodes daily or almost daily)
5. Did you observe any change in the epilepsy course during the time of the pandemic?
 - a. Yes
 - b. No
- 5.1 What change was observed?
 1. more frequent occurrence of seizures
 2. less frequent occurrence of seizures
 3. more severe or longer epilepsy episodes
 4. less severe or shorter epilepsy episodes
 5. occurrence of a new type of seizures

5.2 If a deterioration occurred, in what month has it been observed?

care during pandemic

1 Was the frequency of medical consultations during the pandemic comparable to the frequency before the outbreak?

a. Yes

b. No

1.1 If not, what change occurred?

a. The consultations were more frequent

b. The consultations were less frequent

2. Has the neurologist ever canceled a scheduled appointment?

a. Yes

b. No

2.1 If yes, was a new date for the appointment set?

a. Yes

b. No

3. Was any of medical appointment conducted in a form of a telemedicine?

a. Yes

b. No

3.1 If yes, do you think that a telemedical consultation was as effective as a stationary visit?

a. Yes

b. No

4. Was there a need for urgent hospitalization or medical advice during the pandemic in addition to scheduled, regular visits?

a. Yes

b. No

4.1 If so, did you manage to get help?

a. Yes

b. No

5. Have there been any difficulties in accessing medicines during the pandemic?

a. Yes

b. No

5.1 If so, what problems occurred?

a. Problems with getting to the drugstore

b. Problem with drug availability in the drugstore

c. Other

Additional information

1. Did you observe sleep disturbances (compared to time before pandemic) in your child during the COVID-19 pandemic?

a. Yes

b. No

1.1 If so, what type of sleep disorder did you observe (multiple answers possible)?

a. Shorter sleep time

b. Longer sleep time

c. Insomnia

d. Disturbances in the circadian rhythm

e. Intermittent sleep

f. Difficulty falling asleep

g. Other

2. Did you notice changes (compared to time before pandemic) in your child's behavior during the COVID-19 pandemic?

a. Yes

b. No

2.1 If so, what were they (multiple answers possible)?

a. Irritability

b. Avoiding contact with household member

c. Fear of leaving home

d. Increased frequency of nightmares

e. The onset of physical symptoms such as headache, vomiting, nausea (potentially not related to another disease)

f. Other

3. Did you notice any school problems in your child during COVID-19 pandemic?

a. Yes

b. No

4. Did your child have any infection during the COVID-19 pandemic?

a. Yes

b. No

5. Has your child been infected with the SARS-CoV-2 virus (confirmed by positive PCR test)?

a. Yes

b. No

5.1 If so, what symptoms occurred (multiple answers possible)?

a. Fever above 38 °C

b. Shortness of breath

c. Cough

d. Muscle pain

e. Sore throat

f. Fatigue

g. Excessive sweating

h. Headaches/migraines

i. Taste disturbances

j. Olfactory disturbances

k. Other...

5.2. Did the COVID-19 infection have impact on the epilepsy episodes?

a. Yes

b. No

5.2.1 If so, it involved (multiple choice allowed):

1. An increased frequency of epilepsy episodes?

2. A decreased frequency of epilepsy episodes?

3. An increased intensity of epilepsy episodes?

4. A decreased intensity of epilepsy episodes?

5. An occurrence of new type of epilepsy episodes/new set of symptoms?

References

- [1] Hossain MM, Tasnim S, Sultana A, Faizah F, Mazumder H, Zou L, et al. Epidemiology of mental health problems in COVID-19: a review. *F1000Research* 2020;9:636. <https://doi.org/10.12688/f1000research.24457.1>.
- [2] Galbadage T, Peterson BM, Gunasekera RS. Does COVID-19 spread through droplets alone? *Front Public Heal* 2020;8:1–4. <https://doi.org/10.3389/fpubh.2020.00163>.
- [3] Banerjee D. Social isolation in Covid-19: The impact of loneliness 2020. <https://doi.org/10.1177/0020764020922269>.
- [4] Mahajan V, Singh T, Azad C. Using telemedicine during the COVID-19 pandemic. *Indian Pediatr* 2020;57:658–61. <https://doi.org/10.1007/s13312-020-1895-6>.
- [5] Hadjikitoutis S, Smith PEM. Approach to the patient with epilepsy in the outpatient department. *Postgrad Med J* 2005;81:442–7. <https://doi.org/10.1136/pgmj.2004.029298>.
- [6] Kubota T, Kuroda N. Exacerbation of neurological symptoms and COVID-19 severity in patients with preexisting neurological disorders and COVID-19: A systematic review 2020.
- [7] Asadi-Pooya AA, Simani L, Shahisavandi M, Barzegar Z. COVID-19, de novo seizures, and epilepsy: a systematic review. *Neurol Sci* 2021;42:415–31. <https://doi.org/10.1007/s10072-020-04932-2>.
- [8] Vohora D, Jain S, Tripathi M, Potschka H. COVID-19 and seizures: Is there a link? *Epilepsia* 2020;61:1840–53. <https://doi.org/10.1111/epi.16656>.
- [9] Adan GH, Mitchell JW, Marson T. Epilepsy care in the COVID-19 era. *Clin Med J R Coll Physicians London* 2020;20:e104–6.
- [10] Alkhotani A, Siddiqui MI, Almontashri F, Baothman R. The effect of COVID-19 pandemic on seizure control and self-reported stress on patient with epilepsy. *Epilepsy Behav* 2020.
- [11] Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH, Elger CE, et al. ILAE Official Report: a practical clinical definition of epilepsy. *Epilepsia* 2014;55:475–82. <https://doi.org/10.1111/epi.12550>.
- [12] Beasley TM, Schumacker RE. Multiple regression approach to analyzing contingency tables: post hoc and planned comparison procedures. *J Exp Educ* 1995;64:79–93. <https://doi.org/10.1080/00220973.1995.9943797>.
- [13] Rosengard JL, Donato J, Ferastraru V, Zhao D, Molinero I, Boro A, et al. Seizure control, stress, and access to care during the COVID-19 pandemic in New York

- City: the patient perspective. *Epilepsia* 2020;41–50. <https://doi.org/10.1111/epi.16779>.
- [14] Casassa C, Moss R, Goldenholz DM. Epilepsy during the COVID-19 pandemic lockdown: a US population survey. *Epileptic Disord* 2021;23:257–67. <https://doi.org/10.1684/epd.2021.1259>.
- [15] Assenza G, Lanzone J, Brigo F, Coppola A, Di Gennaro G, Di Lazzaro V, et al. Epilepsy care in the time of COVID-19 pandemic in Italy: risk factors for seizure worsening. *Front Neurol* 2020;11. <https://doi.org/10.3389/fneur.2020.00737>.
- [16] Trivisano M, Specchio N, Pietrafusa N, Calabrese C, Ferretti A, Ricci R, et al. Impact of COVID-19 pandemic on pediatric patients with epilepsy – The caregiver perspective. *Epilepsy Behav* 2020;113:107527. <https://doi.org/10.1016/j.yebeh.2020.107527>.
- [17] Cusinato M, Iannattone S, Spoto A, Poli M, Moretti C, Gatta M, et al. Stress, resilience, and well-being in Italian children and their parents during the COVID-19 pandemic. *Int J Environ Res Public Health* 2020;17:1–17. <https://doi.org/10.3390/ijerph17228297>.
- [18] Carroll N, Sadowski A, Laila A, Hruska V, Nixon M, Ma D, et al. The impact of covid-19 on health behavior, stress, financial and food security among middle to high income canadian families with young children. *Nutrients* 2020;12:1–14. <https://doi.org/10.3390/nu12082352>.
- [19] Araújo LAd, Veloso CF, Souza MdC, Azevedo JMcD, Tarro G. The potential impact of the COVID-19 pandemic on child growth and development: a systematic review. *J Pediatr (Rio J)* 2021:19–21.
- [20] French JA, Brodie MJ, Caraballo R, Devinsky O, Ding D, Jehi L, et al. Keeping people with epilepsy safe during the COVID-19 pandemic. *Neurology* 2020;94:1032–7. <https://doi.org/10.1212/WNL.0000000000009632>.
- [21] Sander JW. The natural history of epilepsy in the era of new antiepileptic drugs and surgical treatment. *Epilepsia* 2003;44:17–20. <https://doi.org/10.1046/j.1528-1157.44.s.1.1.x>.
- [22] Stanuszek A, Wnękowicz E, Kuźniar E, Krakowska K, Gergont A, Kaciński M. Seizure-precipitating factors in relation to medical recommendations: especially those limiting physical activity. *J Child Neurol* 2015;30:1569–73. <https://doi.org/10.1177/0883073815574334>.
- [23] Dono F, Nucera B, Lanzone J, Evangelista G, Rinaldi F, Speranza R, et al. Status epilepticus and COVID-19: a systematic review. *Epilepsy Behav* 2021;118:107887. <https://doi.org/10.1016/j.yebeh.2021.107887>.
- [24] Nikbakht F, Mohammadkhanizadeh A, Mohammadi E. How does the COVID-19 cause seizure and epilepsy in patients? The potential mechanisms. *Mult Scler Relat Disord* 2020;46:102535. <https://doi.org/10.1016/j.msard.2020.102535>.
- [25] Smith P. Telephone review for people with epilepsy. *Pract Neurol* 2016;16:475. <https://doi.org/10.1136/practneurol-2016-001504>. LP – 477.
- [26] Patterson V. Managing epilepsy by telemedicine in resource-poor settings. *Front Public Heal* 2019;7:321. <https://doi.org/10.3389/fpubh.2019.00321>.
- [27] Kissani N, Lengané YTM, Patterson V, Mesraoua B, Dawn E, Ozkara C, et al. Telemedicine in epilepsy: How can we improve care, teaching, and awareness? *Epilepsy Behav* 2020;103:106854. <https://doi.org/10.1016/j.yebeh.2019.106854>.
- [28] Kikuchi K, Hamano S-I, Horiguchi A, Nonoyama H, Hirata Y, Matsuura R, et al. Telemedicine in epilepsy management during the coronavirus disease 2019 pandemic. *Pediatr Int* 2021. <https://doi.org/10.1111/ped.14972>.
- [29] Stafstrom CE, Sun LR, Kossoff EH, Dabrowski AK, Singhi S, Kelley SA. Diagnosing and managing childhood absence epilepsy by telemedicine. *Epilepsy Behav* 2021;115:107404. <https://doi.org/10.1016/j.yebeh.2020.107404>.
- [30] Datta P, Barrett W, Bentzinger M, Jasinski T, Jayagopal LA, Mahoney A, et al. Ambulatory care for epilepsy via telemedicine during the COVID-19 pandemic. *Epilepsy Behav* 2021;116:107740. <https://doi.org/10.1016/j.yebeh.2020.107740>.
- [31] Kubota T, Kuroda N. Association between telemedicine and incidence of status epilepticus during the COVID-19 pandemic. *Epilepsy Behav* 2021;124:108303. <https://doi.org/10.1016/j.yebeh.2021.108303>.
- [32] von Wrede R, Moskau-Hartmann S, Baumgartner T, Helmstaedter C, Surges R. Counseling of people with epilepsy via telemedicine: experiences at a German tertiary epilepsy center during the COVID-19 pandemic. *Epilepsy Behav* 2020;112:107298. <https://doi.org/10.1016/j.yebeh.2020.107298>.
- [33] Fortini S, Espeche A, Caraballo R. Telemedicine and epilepsy: a patient satisfaction survey of a pediatric remote care program. *Epilepsy Res* 2020;165:106370. <https://doi.org/10.1016/j.epilepsyres.2020.106370>.